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Title page:

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Manuscript

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Question

A 25-year-old Eritrean woman was admitted with a four week history of abdominal pain and weight loss of 10 kg without diarrhoea and without family history of neoplasia. Physical examination was significant for mild tenderness over the right abdomen. Hemoglobin was decreased with 96 g/l (normal 120-160 g/l) and CRP elevated with 114 mg/l (n < 8mg/l) with normal white cell count. Contrast-enhanced CT of the chest and abdomen showed a polypoid hyperdense intraluminal mass measuring 25 mm in the ascending colon (Fig. A) without metastases. Colonoscopy revealed a pedunculated polyp with a head size of 25 mm with ulcerated surface and a stalk size of 10 mm in the ascending colon (Fig. B). The polyp was lifted after submucosal injection into the stalk with 1:100'000 adrenaline, saline, indigocarmine and succinylated gelatine (Fig. C). Hot snare (25mm snare) polypectomy and bleeding prevention with clips were successfully performed with retrieval of the polyp for histopathological examination (Fig. D, E).

What is the diagnosis?

Answer

Histology revealed an unencapsulated tumor consisting of ovoid spindle cells with eosinophilic cytoplasm arranged in a loose fascicular growth pattern set in a collagenous background with a mild lymphocytic inflammatory component. The mitotic count was up to 4/10 HPF, without tumour necrosis and no high grade cytological atypia (Fig F, G). Immunohistochemistry showed the tumour cells to be diffusely and strongly positive for S100 (Fig. H) and CD34 (Fig. I) whereas DOG1, CD117, desmin, alpha SMA, caldesmon, MelanA, HMB-45 amongst others were negative. Molecular analysis detected a NTRK1 (neurothrophic receptor tyrosine kinase) -TPM3 gene fusion by new genome sequencing (using Oncomine Focus Assay, Thermo Fisher).

This case is the first report of a novel group of NTRK-rearranged spindle cell neoplasms in the colon, defined by S100 / CD34 co-expression and a NTRK1-TPM3 gene fusion. Suurmeijer et al. (1) reported this heterogeneous entity with at most low malignant potential in soft tissue tumors. In this case series (1) only one tumor was detected in the gastrointestinal tract (stomach). Wong et al (2) also reports different locations like soft tissue, liver, uterus or lung with various outcome of NTRK-rearranged spindle cell neoplasms. The proto-oncogenes NTRK encode the TRK (tropomyosin receptor kinases) proteins and specific and highly effective TRK inhibitors targeted therapies for adults and children exist (3).

This case was presented at our interdisciplinary tumor-board with the recommendation of oncological resection. Laparoscopic right hemicolectomy with complete mesocolic excision was performed without any signs of peritoneal seeding or other abnormalities. No residual tumor could be detected after hemicolectomy.

No data are available regarding prognosis and management of this tumor entity. Because of low mitotic rate (4 mitosis per 10 HPF) without metastases, this tumor was classified as low grade in our interdisciplinary sarcoma board. According to the surveillance of low grade sarcoma of the soft tissue, surveillance with CT (every 6 months for two years and yearly for 5 years) and yearly colonoscopy (for 5 years) were recommended.

References

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